

CGATGTCTGCACAAGGCTGTCACTCAGGTGGCAGTGGCTGACACGTGGCCGGGCAGCTCTGC
 TGCTGCGGCGCGAAGTCGAGAGGCGGCGGGTCCGTGGCGCGCGCTCGCATTGCTCCGAGGC
 TCCGAGCGGCGATACGGGCGGGCGCCGACGGCAGGGTCTCCATGCCGCGCGTGGGGCGGGC
 CGCTGATGGAGCGCGCCACCCGGCCCGGGCCGCGCGCTGCTGCTGCTTCTGTTCTTGCTG
 CTGGGCTGCGCGGCGGGGATCTCTGCGGTGCGCGCCCGCCCGCAGTTTGCTTGCTCCCGCGTC
 GGAGACAGTGTGTTGGCTTAGGGGCAGCGGCCGCCCCGACTTCGGCCGCGCGGGTGCCTGCGG
 TGGCAACGGCCGAAGTGACCGTGAGGACGCCGAGGCATTGCCGGCTGCCGCTGGCGAACCG
 GAGTCACGCGCGACGGAGCCCCGATGACGACGTGGAACCTGCGGCCTCGCGGCAGGTCCTTGGT
 AATCATCAGCACTTTAGATGGACGAATCGCTGCACTGGATGCCGAGAATGATGGGAAAAAGC
 AGTGGGATTTGGACGTGGGGTCTGGTTCTTGGTTTCATCTAGCCTCAGCAAGCCAGAGGTG
 TTTGGGAACAAGATGATCATCCCCCTCCCTGGATGGAGACCTCTTCCAGTGGGACCGGGACCG
 AGAGAGCATGGAGGCCGTCCCCTTACGGTGGAGTCCCTGCTCGAATCTTCTACAAGTTTG
 GAGATGATGTTGTTCTGGTTGGAGGGAAATCTCTGATTACATACGGACTCAGTGCTTACAGT
 GGAAAGCTGAGGTATATCTGTTCTGCCTTGGGATGTGCGCGATGGGATAGTGATGAAATGGA
 AGAAGAGGAAGACATCTTGCTTCTGCAGCGTACGCAGAAGACTGTGCGAGCTGTGCGGCCTC
 GAAGCGGCAGTGAGAAGTGGAATTTAGTGTGGCCACTTTGAACTTCGGTATATTCCAGAC
 ATGGAACTAGAGCCGGATTTCATTGAAAGCACCTTTAAACCGGGTGGAAACAAAGAAGACTC
 TAAAATTATTTAGATGTGGAAGAACAAGAAGCCACCATGCTGGACACAGTGATAAAAGTTT
 CCGTTGCTGATTGGAAGGTGATGGCGTTTAGTAGGAAGGGAGGCCGCTGGAATGGGAGTAC
 CAGTTTTGTACTCCCATCGCGTCCGCTGGCTGGTGAGGGATGGCAAGGTGATCCCCATCAG
 CCTGTTTGATGATACAAGTTACACAGCCAGCGAAGAAGCCTTGGGAGACGAAGAAGACATTG
 TAGAGGCTGCTCGGGGAGCCACAGAGAACAGCGTGTACTTAGGGATGTACAGAGGCCAGCTG
 TACCTGCAGTCGTCCGTGAGGGTCTCAGAAAAGTTCCCTACAAGCCCAAAGGCCCTTGAGTCT
 TGTAATGGCGAAAATGCAATTATTCTCTGCCGACGATCAAATGGAAGCCCTTAATCCATT
 CTCCTTCTAGGACTCCTGTCTTGGTTGGGTCTGATGAATTTGACAAATGTCTAAGTAATGAT
 AAGTATTTCCACGAAGAATACAGTAATGGTGCATTTCAATCCTCCAGTATCCATACGATAA
 CGGTTACTATCTGCCATACTACAAGAGAGAAAGGAATAAGCGGAGCACGCAGATCACAGTCA
 GGTTCCCTGGACAGCCCCCACTACAGCAAGAACATCCGCAAGAAGGACCCTATCCTCCTGCTG
 CACTGGTGGAAAGGAGATATTCGGGACGATCCTGCTTTGCATCGTAGCCACGACCTTCATCGT
 GCGCAGGCTTTTCCATCCTCAGCCCCACAGGCAGCGGAAGGAGTCTGAAACTCAGTGCCAGA
 CTGAAAGTAAATACGACTCCGTGAGTGCCGATGTGAGTGACAACAGCTGGAATGACATGAAG
 TACTCAGGATACGTATCCCGATATCTAACAGATTTTGAGCCAATTCAGTGCATGGGTCTGG
 TGGCTTTGGCGTTGTCTTTGAAGCTAAAAACAAAGTAGATGACTGCAATTACGCTATCAAGA
 GGATCCGGCTCCCCAACAGGGAGTTGGCACGGGAGAAGGTAATGCGGGAAGTTAAAGCCTTG
 GCTAAGCTGGAACACCCAGGCATTGTGAGGTATTTCAACGCCTGGCTGGAAACCCACCAGA
 GAAGTGGCAAGAAGAGATGGATGAGATCTGGCTCAAAGACGAAAGCACAGACTGGCCGCTCA
 GCTCCCCCTAGCCCGATGGATGCCCCATCTGTTAAGATCCGAAGGATGGATCCYTTCTCTACA
 AAAGAGCAGATCGAAGTCATAGCTCCTTCTCCTGAAAGAAGTCGGTCTTTCTCGGTGGGCAT
 TTCCTGTGGCCAGACAAGCTCATCGGAGAGCCAGTTCTCTCCCCTGGAGTTCTCAGGGACAG
 ACTGCGGAGACAACAGTGACTCAGCGGACGCAGCCTACAACCTCCAGGACAGTTGCCTGACG
 GACTGCGAGGACGTGGAAGATGGCACCGTGGACGGCAATGACGAGGGACACTCCTTTGAACT
 TTGTCCGTCCGAAGCTTCTCCCTATACCCGGTCTAGGGAAGGAACGTCCTCCTCCATAGTGT
 TTGAGGACTCTGGCTGCGGCAACGCGTCCAGTAAGGAGGAGCCAGAGGGAACCGGCTGCAT
 GATGGCAACCATTATGTTAATAAGCTAACTGATCTCAAGTGCTCCAGCAGCAGGTCTTCTTC
 AAGAACACTGTGGGCCAGCTCCAGCCCAGCTCCCCCAAGGTGTATCTGTGAAGCCACCACCT
 TGTCTACCTCCCCTACCAGGCCAACCACTCTAAGCTTGGATTTACCAACATTGATGCAG

FIGURE 1A(1)

CTGTGCAGGAAGGAGAACCTCAAAGACTGGATGAACCGGCGCTGCAGCTTGGAGGACCGGGA
GCACGGCGTGTGCCTGCACATCTTCCTGCAGATCGCAGAGGCAGTGGAGTTCCTGCACAGCA
AGGGACTCATGCACAGGGACCTCAAGCCTTCCAACATATTCTTCACAATGGATGATGTGGTC
AAGGTTGGGGACTTTGGACTGGTGA CTGCTATGGACCAAGATGAAGAAGAGCAGACTGTTCT
GACTCCAATGCCAGCCTATGCTACGCACACGGGACAAGTAGGGACCAAGCTATACATGAGCC
CAGAGCAGATTCATGGAAACA ACTACTCCCATAAAGTGGACATCTTCTCTTTAGGCTTGATT
CTGTTTGAACTCCTCTACCCATT CAGCACCCAGATGGAACGAGTCCGGATTTTAACTGATGT
CAGAAATCTCAAGTTTCTCTACTGTTCACTCAGAAATATCCCCAAGAGCATATGATGGTTC
AAGACATGCTCTCTCCATCCCCACGGAGCGGCCTGAAGCCACAGACATCATTGAAAATGCC
ATATTTGAGAACTTGGAGTTTCCCGGGAAAACGGTCTGAGACAGCGGTCCCGCTCCATGAG
TTCATCTGGAACAAAACATTC CAGACAGCCCAGCTGCTCGTACAGCCCACTGCCTGGCAACT
AGCCCTCAGCTGCCCTCGAAGGTGGCAGAGCAGGCACCCTGAGGAACATGGCTCTCCACAGC
GGTGGACTCAGATTTTATGCTTTGATCAGTTGGACTCGGGACCAATTTTTCTAAGTCAGACT
GGATCACGGGCCTAACCAGTTTGATCTTAACTGAACTTCAAGGAAAGGGCTGTGTAAAGGA
CACATGAACTTGTTGCTTGTTCGGTGTCCCAAGACTAGCTGGTCAGCTTAGAACCTTCACTTT
TCACCAGGCGGTAGAAGAGATCCTCAAATGGTCTGAACTGGAAATGTCTTTAAAGCACAAAA
GTGTAAAAGACCCTCTCACATGGGAACTACATGTTCTAGAAACGTGCTTTCTAGAGATACAA
GGGTGATTTTGGAAGTGGTTGTTATAAAGCTGACTTCATTTTTTTCCCTGGTGAGCCGTGAC
CCATCTGCACTAATTTGCAAGGCACATAGCACAAAGCTGGGTGCGCCATTTATGTCGGTAGTGT
CATAGTCTGCAGCAGTGAATAGCGTCATTCTTCAGGTGGTCTAGGGAGCGCGAAAAGCTTTT
TTGTACTTTTTTACCTCCAATAATGGGAAAATGAAGCTTTTAGGTATTGGTCAAAAGATCTGA
TTTGAGAGTTTTTGGGTTTTTTTTTTTAAAGTGCAGTAGGAAATGGATTATCTATTACAAC TAAC
TTCTTCAATTATGGAATTTTTATCCTAGTAGAATTCTGTCTTAAATGTAATACTACAAGTGG
GTACATTCCCCAAACTGATTATAGATAAGTTTAATCATCTCAACTTGCTAACATGTTTTCA
TTTTTCTGTAAATACGTTTATTTTTTATTTATAAAAATTCTGAAATCAATCCATTTGGGTT
GGTGGTGTACAGAACGCACGTAAGTGTGATAACTATTATGACTTCTTTCAAGTCTAAATGAT
TTAATAAAAAAATTTTAAATTAAAAA AAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:1)

FIGURE 1A(2)

MERATRPGPRALLLLFLLLGCAAGISAVAPARSLAPASETVFGLGAAAAP TSAARVPAVA
TAEVTVEDAEALPAAAGEPESRATEPDDDVELRPRGRSLV IISTLDGRIAALDAENDGKKQW
DLVDVSGSLVSSSLSKPEVFGNKMIIPSLDGDLFQWDRDRESMEAVPFTVESLLESSYKFGD
DVVLVGGKSLITYGLSAYSGKLRYICSA LGCRRWDSDEMEEEEDILLLQRTQKTVRAVGPRS
GSEKWNFSVGHFELRYIPDMETRAGFIESTFKPGGNKEDSKIISDVEEQEATMLD TVIKVSV
ADWKVMAFSRKGGRLWEYQFCTPIASAWLVRDGKVIPI SLFDDTSYTASEEALGDEEDIVE
AARGATENSVYLGMYRGQLYLQSSVRVSEKFPTSPKALESVNGENAI IPLPTIKWKPLIHSP
SRTPVLVGSDEFDKCLSNDKYSHEEYSNGALSILQYPYDNGYYLPYYKRERNKRSTQITVRF
LDSPHYSKNIRKKDPILLHWWKEIFGTILLCIVATTFIVRRLFHPQPHRQRKESETQCQTE
SKYDSVSADVSDNSWNDMKYSGYVSRYLTDFEPIQCMGRGGFGVVFEAKNKVDDCNYAIKRI
RLPNRELAREKVMREVKALAKLEHPGIVRYFNAWLETPEKWQEEMDEIWLKDESTDWPLSS
PSPMDAPSVKIRMDPFSTKEQIEVIAPSPERSRFSVSGISCGQTSSSESQFSPLEFSGTDC
GDNSDSADAAYNLQDSCLTDCEDVEDGTVDGNDEGH SFELCPSEASPYTRSREGTSSSIVFE
DSGCGNASSKEEPRGNRLHDGNHYVNKLTDLCSSSRSSSEATTLSTSPTRPTTSLDFTKN
TVGQLQPSSPKVYLYIQMQLCRKENLKDWMNRCSLEDREHGVCLHIFLQIAEAVEFLHSGK
LMHRDLKPSNIFFTMDDVVKVGDFGLVTAMDQDEEEQTVLTPMPAYATHTGQVGTKLYMSPE
QIHGNNYSHKVDIFSLGLILFELLYPFSTQMERVRILT DVRNLKFPLLFTQKYPQEHMMVQD
MLSPSPTERPEATDI IENAI FENLEFPGKTVLRQSRSMSSSGTKHSRQPSCSYSP LPGN
(SEQ ID NO:2)

FIGURE 1B

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

CGATGTCTGCACAAGGCTGTCACTCAGGTGGCAGTGGCTGACACGTGGCCGGGCAGCTCT
GCTGCTGCGGCGCGAAGTCGAGAGGCGGCGGGTCCGTGGCGCGCGCTCGCATTGCTCCG
AGGCTCCGAGCGGCGATACGGGCGGGCGCGACGGCAGGGTCTCCATGCCCGCGCTGGG
GCGGGCCGCTGATGGAGCGGCCACCCGGCCCGGGCCGCGCGCGCTGCTGCTGCTTCTGT
TCCTGCTGCTGGGCTGCGCGCGGGGATCTCTGCGGTGCGCGCCCGCCGCGAGTTTGCTTG
CTCCCGCGTTCGAGACAGTGTGTTGGCTTAGGGGACGGCGCGCCCGGACTTCGGCCGCGC
GGGTGCTGCGGTGGCAACGGCCGAAGTGACCGTGGAGGACGGCGAGGCATTGCCGGCTG
CCGCTGGCGAACCGGAGTCACGCGCGACGGAGCCCGATGACGACGTGGAAGTGC GGCCCTC
GCGGCAGGTCTTTGGTAATCATCAGCACTTTAGATGGACGAATCGCTGCACTGGATGCCG
AGAATGATGGGAAAAAGCAGTGGGATTGACGTGGGGTCTGGTTCTTTGGTTTTCATCTA
GCCTCAGCAAGCCAGAGGTGTTTGGGAACAAGATGATCATCCCCCTCCCTGGATGGAGACC
TCTTCCAGTGGGACCGGGACCGAGAGAGCATGGAGGCCGTCCCCCTCACGGTGGAGTCCC
TGCTCGAATCTTCTACAAAGTTTGGAGATGATGTGTTCTGGTTGGAGGGAAATCTCTGA
TTACATACGGACTCAGTGCTTACAGTGGAAAGCTGAGGTATATCTGTTCTGCCTTGGGAT
GTCGCCGATGGGATAGTGATGAAATGGAAGAAGAGGAAGACATCTTGCTTCTGCAGCGTA
CGCAGAAGACTGTGCGAGCTGTGCGGCCCTCGAAGCGGCAGTGAGAAGTGAATTTAGTG
TTGGCCACTTTGAACTTCGGTATATTCCAGACATGAAACTAGAGCCGGATTCAATTGAAA
GCACCTTTAAACCGGGTGGAAACAAAGAAGACTCTAAATATTATTCAGATGTGGAAGAAC
AAGAAGCCACCATGCTGGACACAGTGATAAAAGTTTCCGTTGCTGATTGGAAGGTCATGG
CGTTTAGTAGGAAGGGAGGCCGCTGGAATGGGAGTACCAGTTTGTACTCCCATCGCGT
CCGCTTGGCTGCTGAGGGATGGCAAGGTCTATCCCCATCAGCCTGTTTGATGATACAAGTT
ACACAGCCAGCGAAGAAGCCTTGGGAGACGAAGAAGACATGTAGAGGCTGCTCGGGGAG
CCACAGAGAACAGCGTGTACTTAGGGATGTACAGAGGCCAGCTGTACCTGCAGTCGTCCG
TCAGGGTCTCAGAAAAGTTCCCTACAAGCCCAAGGCCTTGGAGTCTGTAAATGGCGAAA
ATGCAATTATTCTCTGCCGACGATCAAATGGAAGCCCTTAATCCATTCTCCTTCTAGGA
CTCCTGTCTTGGTTGGGTCTGATGAATTTGACAAATGTCTAAGTAATGATAAGTATTCCC
ACGAAGAATACAGTAATGGTGCACTTTCAATCCTCCAGTATCCATACGATAACGGTTACT
ATCTGCCATACTACAAGAGAGAAAGGAATAAGCGGAGCACGCAGATCACAGTCAGGTTCC
TGGACAGCCCCACTACAGCAAGAACATCCGCAAGAAGGACCCTATCCTCCTGCTGCACT
GGTGAAGGAGATATTCGGGACGATCCTGCTTTGCATCGTAGCCACGACCTTCATCGTGC
GCAGGCTTTTCCATCCTCAGCCCCACAGGCAGCGAAGGAGTCTGAAACTCAGTGCCAGA
CTGAAAGTAAATACGACTCCGTGAGTGCCGATGTGAGTGACAACAGCTGGAATGACATGA
AGTACTCAGGATACGTATCCCGATATCTAACAGATTTTGAGCCAATTCAGTGATGGGTC
GTGGTGGCTTTGGCGTTGTCTTTGAAGCTAAAAACAAAGTAGATGACTGCAATTACGCTA
TCAAGAGGATCCGGCTCCCAACAGGGAGTTGGCACGGGAGAAGGTAATGCGGGAAGTTA
AAGCCTTGGCTAAGCTGGAAACACCCAGGCATTGTGAGGTATTTCAACGCCTGGCTGGAAA
CCCCACCAGAGAAGTGGCAAGAAGAGATGGATGAGATCTGGCTCAAAGACGAAAGCACAG
ACTGGCCGCTCAGCTCCCCTAGCCGATGGATGCCCCATCTGTTAAGATCCGAAGGATGG
ATCCYTTCTCTACAAAAGAGCAGATCGAAGTCATAGCTCCTTCTCCTGAAAGAAGTCGGT
CTTTCTCGGTGGGCATTTCTGTGGCCAGACAAGCTCATCGGAGAGCCAGTTCTCTCCCC
TGGAGTTCTCAGGGACAGACTGCGGAGACAACAGTGACTCAGCGGACGCAGCCTACAACC
TCCAGGACAGTTGCCTGACGGACTGCGAGGACGTGGAAGATGGCACCGTGGACGGCAATG
ACGAGGGACACTCCTTTGAACTTTGTCCGTCCGAAGCTTCTCCC [TATACCCGGTCTAGG

FIGURE 2A(1)

10005983-110701

GAAGGAACGTCCTCCTCCATAGTGTGTTGAGGACTCTGGCTGCGGCAACGCGTCCAGTAAG
 GAGGAGCCCAGAGGGAACCGGCTGCATGATGGCAACCATTATGTTAATAAGCTAACTGAT
 CTC AAGTGCTCCAGCAGCAGGTCTTCTTCAGAAGCCACCACCTTGTCTACCTCCCCTACC
 AGGCCAACCCTCTAAGCTTGGATTTACCAAGAACACTGTGGGCCAGCTCCAGCCCAGC
 TCCCCAAGGTGTATCTGTACATTAGATGCAGCTGTGCAGGAAGGAGAACCTC] AAAGA
CTGGATGAACCGGCGCTGCAGCTTGGAGGACCGGGAGCACGGCGTGTGCCTGCACATCTT
CCTGCAGATCGCAGAGGCAGTGGAGTTCTCTGCAC [AGCAAGGGACTCATGCACAGGGACC
 TCAAG] CCTTCCAACATATTCTTCACAATGGATGATGTGGTCAAGGTTGGGGACTTTGGA
 CTGGTGACTGCTATGGACCAAGATGAAGAAGAGCAGACTGTTCTGACTCCAATGCCAGCC
 TATGCTACGCACACGGGACAAGTAGGGACCAAGCTATACATGAGCCCAGAGCAGATTTCAT
 GGAAACAACTACTCCCATAAAGTGGACATCTTCTCTTTAGGCTTGATTCTGTTTGAACCTC
 CTCTACCCATTAGCAGCCAGATGGAACGAGTCCGGATTTTAACTGATGTCAGAAATCTC
 AAGTTTCTCTACTGTTCACTCAGAAATATCCCCAAGAGCATATGATGGTTCAAGACATG
 CTCTCTCCATCCCCCAGGAGCGGCGCTGAAGCCACAGACATCATTGAAAATGCCATATTT
 GAGAACTTGGAGTTTCCCGGAAAAACGGTCTGAGACAGCGGTCCCGCTCCATGAGTTCA
 TCTGGAACAAAACATTCCAGACAGCCCAGCTGCTCGTACAGCCCACTGCCTGGCAACTAG
 CCCTCAGCTGCCCTCGAAGTGGCAGAGCAGGCACCCTGAGGAACATGGCTCTCCACAGC
 GGTGGACTCAGATTTTATGCTTTGATCAGTTGGACTCGGGACCAATTTTCTAAGTCAGA
 CTGGATCACGGGCCTAACCCAGTTTGATCTTAACTGAACTTCAAGGAAAGGGCTGTGTAA
 AGGACACATGAACTTGTGTGCTTGTGCGGTGTCCCAAGACTAGCTGGTCAGCTTAGAACCTT
 CACTTTTACCAGGCGGTAGAAGAGATCCTCAAATGGTCTGAACTGGAAATGTCTTTAAA
 GCACAAAAGTGTAAGAGACCCCTCTCACATGGGAACTACATGTTCTAGAAACGTGCTTTCT
 AGAGATACAAGGGTGATTTTGAAGTGGTTGTTATAAAGCTGACTTCATTTTTTCCCTG
 GTGAGCCGTGACCCATCTGCACTAATTTGCAAGGCACATAGCACAAAGCTGGGTGCGCATT
 TATGTCGGTAGTGTCATAGTCTGCAGCAGTGAATAGCGTCATTCTTCAGGTGGTCTAGGG
 AGCGCGAAAAGCTTTTTTGTACTTTTTACCTCCAATAATGGGAAAATGAAGCTTTTAGGT
 ATTGGTCAAAAGATCTGATTTGAGAGTTTTGGGTTTTTTTTTTAAGTCAGTAGGAAATG
 GATTATCTATTACAATACTTCTTCAATTATGGAATTTTTATCCTAGTAGAATTCTGTC
 TTAATGTAATACTACAAGTGGGTACATTCCCCAACTGATTATAGATAAGTTTAATCA
 TCTCAACTTGCTAACATGTTTTCATTTTTCTGTAAATACGTTTATTTTTTATTTATAAA
 AATTCTGAAATCAATCCATTTGGGTGGTGGTGTACAGAACGCACGTAAGTGTGATAACT
 ATTATGACTTCTTCAAGTCTAAATGATTTAATAAAAAAATTTTAAATTAAAAAATAAA
 AAAAAAAAAAAAAA

FIGURE 2A(2)

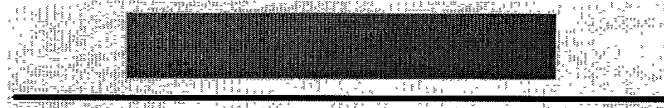
Gene Sequence Structure *

2874 bp

Sequence Deleted

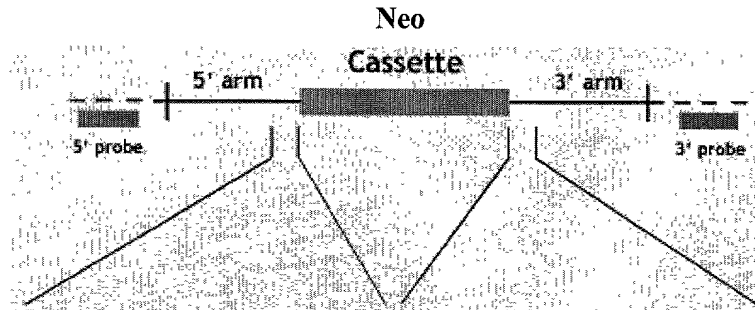
2972 bp

Size of full-length
cDNA: 4510 bp



Targeting Vector* (genomic sequence)

Arm Length:
5': 2.4 kb
3': 1.3 kb



— Targeting Vector
- - - Endogenous Locus
* Not drawn to scale

5' > ACCATTATGTTAATAAGCTAA
CTGATCTCAAGTGCTCCAGCAGCA
GGTCTTCTTCAGAAGCCACCACCT
TGTCTACCTCCCCTACCAGGCCAA
CCACTCTAAGCTTGGATTTCACCA
AGAACTGTGGGCCAGCTCCAGC
CCAGCTCCCCCAAGGTGTATCTGT
ACATTGAGATGCAGCTGTGCAGGA
AGGAGAACCTC < 3' (SEQ ID
NO: 3)

5' > AGCAAGGGACTCATGCACGGG
ACCTCAAGGTCTGTAGCCAGAGGC
GGCCACGCCGGGCTTTGGGTGTGC
CCTGGGGTTCAGAGCAGAGGTCGG
GGAAGGAAGCAGGGAAGGAAGAAG
TCTCATATGTAAAGGCTCAGGCA
GACTGTGCATCTTCCTTTACGGCC
TGTTTATTTTGTCTTACTGTAAA
CACTGTTTCCA < 3' (SEQ ID
NO: 4)

FIGURE 2B

Phenotypic Data Summary - Metrazol

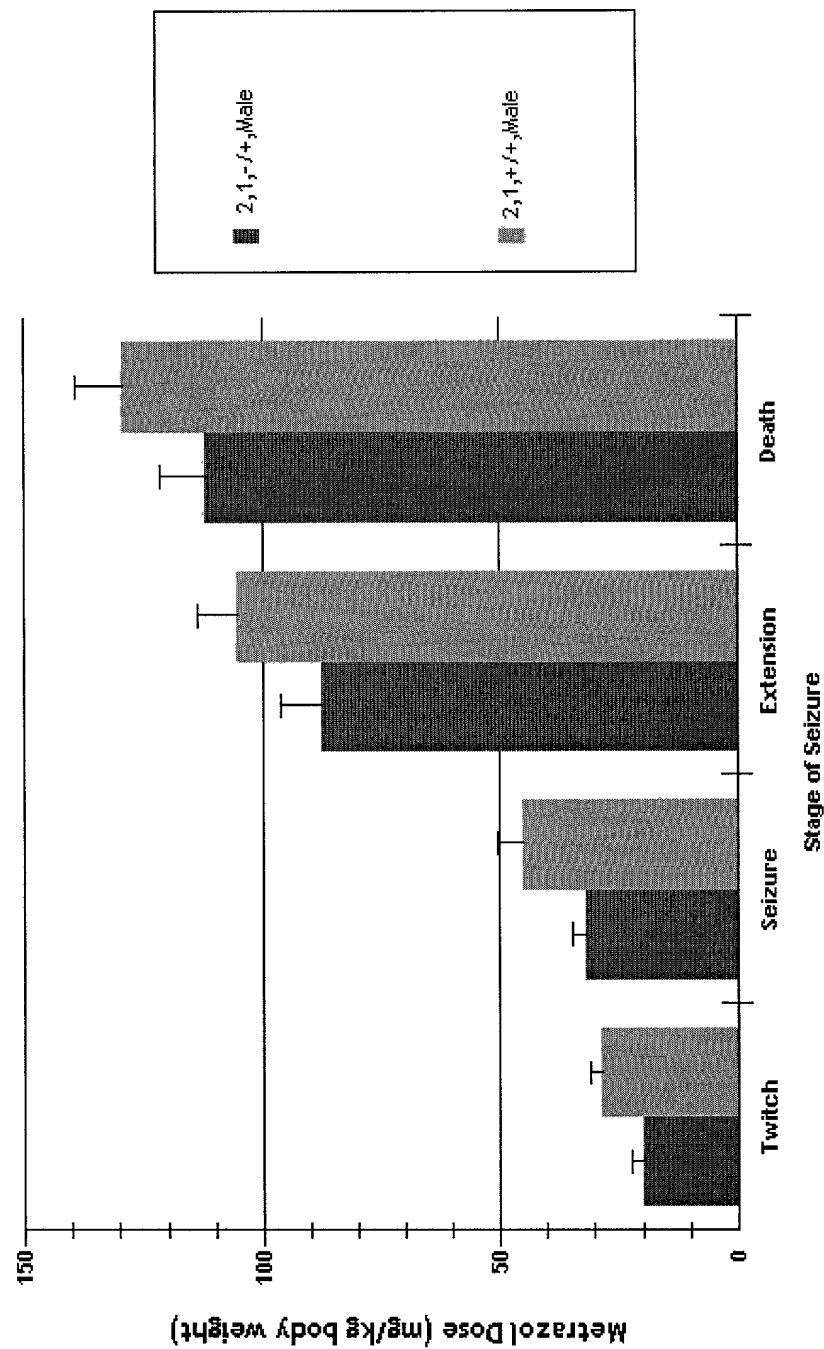


FIGURE 3